



PATHOGENS CAUSING MENINGITIS AND THEIR JOURNEY IN TO THE BRAIN

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ABSTRACT

C N S infections are caused by Protozoans, Bacterial, Viral, Prionic, Fungal and post infectious diseases of Nervous systems. Malaria, Primary Amoebic meningoencephalitis and toxoplasmosis protozoans cause encephalitis. Tuberculosis, Leprosy, Neurosyphilis, Bacterial meningitis, late stage of Lyme disease, Brain abscess, Neuro Borreliosis, Streptococcus pneumoniae, Streptococcus agalactiae, Neisseria meningitidis, Haemophilus influenza, Listeria monocytogenes cause bacterial meningitis. Viruses like Estereon equine encephalitis, Saint Louis, West Nile, Japanese, Herpes simplex virus, Rabies virus, California virus, Varicella virus, Measles encephalitis, Poliomyelitis, Slow virus encephalitis cause meningitis. Creutzfeldt-Jacob disease, Fatal familial insomnia and Kuru etc Pr ionic diseases cause meningitis. Cryptococcal meningitis, brain abscess, spinal epidermal infections also produce meningitis. Bacterial meningitis is very serious and deadly. Death can occur in as little as few hours. Most people recover from meningitis. However permanent disabilities can result from infection.

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INTRODUCTION

Bacterial meningitis is very serious and can be deadly. Death can occur in as little as a few hours. Most people recover from meningitis. However, permanent disabilities (such as brain damage, hearing loss, and learning disabilities) can result from the infection.

There are several types of bacteria that can cause meningitis. Leading causes in the United States include Streptococcus pneumoniae, Group B Streptococcus, Neisseria meningitidis, Haemophilus influenza and Listeria monocytogenes

On average, bacterial meningitis caused about 4,100 cases and 500 deaths in the United States each year between 2003 and 2007. [1]

Bacterial meningitis continues to be a significant cause of morbidity and mortality worldwide. Vaccination has greatly contributed to the current decline in the number of cases for the three most common meningeal pathogens (Haemophilus influenzae, Neisseria meningitidis, and Streptococcus pneumoniae). (3) Young infants who have meningitis may present with nonspecific clinical manifestations. S.

pneumoniae and N. meningitidis remain the most common causes of bacterial meningitis in the infant and child, and GBS continues to be the most common neonatal pathogen. Empiric therapy for suspected bacterial meningitis in a non-neonate includes a combination of parenteral vancomycin and either cefotaxime or ceftriaxone. (7)

Tuberculous meningitis is also known as TB meningitis or tubercular meningitis. Tuberculous meningitis is Mycobacterium tuberculosis infection of the meninges-the system of membranes which envelop the central nervous system. (14) (15)

Mycobacterium tuberculosis of the meninges is the cardinal feature and the inflammation is concentrated towards the base of the brain. (16) When the inflammation is in the brain stem subarachnoid area, cranial nerve roots may be affected. The symptoms will mimic those of space-occupying lesions. (17)

Blood-borne spread certainly occurs, presumably by crossing the blood-brain barrier; but a proportion of patients may get TB meningitis from rupture of a cortical focus in the brain.

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(18)an even smaller proportion get it from rupture of a bony focus in the spine. (19)

Viral meningitis is the most common type of meningitis, an inflammation of the tissue that covers the brain and spinal cord. It is often less severe than bacterial meningitis, and most people get better on their own (without treatment). However, it's very important for anyone with symptoms of meningitis to see a healthcare provider right away because some types of meningitis can be very serious, and only a doctor can determine if you have the disease, the type of meningitis, and the best treatment, which can sometimes be lifesaving. Babies younger than 1 month old and people with weakened immune systems are more likely to have severe illness from viral meningitis.(2)

In the United States, the annual number of central nervous system (CNS) infections that occur as a result of viral agents far exceeds that of infections caused by bacteria, yeast, molds, and protozoa combined. The recent incursion of West Nile virus (WNV) into North America has led to a dramatic change in the incidence and epidemiology of summer-associated viral CNS disease. As a result of increased testing for WNV, lesser known viral causes of CNS infection have been identified.(4) Viral meningitis, also known as aseptic meningitis, is a type of meningitis due to a viral infection. It results in inflammation of the meninges (the membranes covering the brain and spinal cord). Symptoms commonly include headache, fever, sensitivity to light, and neck stiffness. (20)

Viruses are the most common cause of aseptic meningitis.(21) Most cases of viral meningitis are caused by enteroviruses (common stomach viruses).(22) (23) (24) However, other viruses can also cause viral meningitis. For instance, West Nile virus, mumps, measles, herpes simplex types I and II, varicella, and lymphocytic choriomeningitis (LCM) virus.(23) (25) Based on clinical symptoms, viral meningitis cannot be reliably differentiated from bacterial meningitis, although viral meningitis typically follows a more benign clinical course. Viral meningitis has no evidence of bacteria present in cerebral spinal fluid (CSF). Therefore, lumbar puncture with CSF analysis is often needed to identify the disease.(26)

In most causes there is no specific treatment, with efforts generally aimed at relieving symptoms (headache, fever, or nausea) (27)A few viral causes, such as HSV, have specific treatments.

In the United States viral meningitis is the cause of greater than half of all cases of meningitis.(28)From 1988–1999, about 36,000 cases occurred a year. (29)While the disease can occur in both children and adults it is more common in children.(20) Viral meningitis and encephalitis occur at all stages of life. They may represent disease at its primary site of replication (e.g. rabies) or be part of an infection syndrome (e.g. HIV). A large proportion of cases go unconfirmed by laboratory diagnosis despite use of all available laboratory techniques.(5) Fungal meningitis is rare and usually caused by fungus spreading through blood to the spinal cord. Although anyone can get fungal meningitis, people with weakened immune systems, like those with an HIV infection or cancer, are at increased risk.(2)

The most common cause of fungal meningitis for people with weak immune systems is *Cryptococcus*. This disease is one of

the most common causes of adult meningitis in Africa.Fungal meningitis tends to be a subacute or chronic process; however, it may be just as lethal as bacterial meningitis if untreated. There are many similarities between the pathogenic fungi. Most of the fungi are aerosolized and inhaled, and initiate a primary pulmonary infection which is usually self-limited. Hematogenous dissemination may follow the initial infection, with subsequent involvement of the CNS.(6)

Various parasites can cause meningitis or can affect the brain or nervous system in other ways. Overall, parasitic meningitis is much less common than viral and bacterial meningitis.(2)

Some parasites can cause a rare form of meningitis called eosinophilic meningitis, eosinophilic meningoencephalitis, or EM, with increased levels of eosinophils (a type of white blood cell) in the fluid around the brain and spinal cord (the cerebrospinal fluid; CSF). EM also can be caused by other types of infections (not just by parasites) and can have noninfectious causes, such as medications.(2)

Naegleria fowleri (commonly referred to as the “brain-eating amoeba” or “brain-eating ameba”), is a free-living microscopic ameba*, (single-celled living organism). It can cause a rare** and devastating infection of the brain called primary amebic meningoencephalitis (PAM). The ameba is commonly found in warm freshwater (e.g. lakes, rivers, and hot springs) and soil. *Naegleria fowleri* usually infects people when contaminated water enters the body through the nose. Once the ameba enters the nose, it travels to the brain where it causes PAM, which is usually fatal. Infection typically occurs when people go swimming or diving in warm freshwater places, like lakes and rivers. In very rare instances, *Naegleria* infections may also occur when contaminated water from other sources (such as inadequately chlorinated swimming pool water or heated and contaminated tap water) enters the nose (8 - 11) You cannot get infected from swallowing water contaminated with *Naegleria*.

Toxoplasma gondii is an opportunistic pathogen that causes neurologic and extraneurologic manifestations in immunosuppressed patients. Encephalitis and intracranial mass lesions are easily recognized as typical manifestations of toxoplasmosis. However, meningitis caused by *T. gondii* is a rare condition with very few cases described in the literature. We present the case of a heart transplant recipient who developed toxoplasmic encephalitis associated with meningitis.(12)

Malaria is one of the most common treatable and preventable infectious diseases in the world; and 300–500 million malaria cases occur annually, leading to 1.5–2.7 million deaths in tropical countries. About one-third of these cases occur in Asia. In hyperendemic area, most of the children acquire infection by the age of 5 years. Children younger than 6 months enjoy immunity from their mothers. In India the disease occurs in all the age groups.(13)

Prion diseases of the CNS may present as sporadic, rapidly progressive dementia associated with myoclonus (Creutzfeldt-Jakob disease, CJD), or less commonly as familial forms of rapidly progressive dementia (familial CJD); cerebellar degeneration (Gerstmann-Straussler-Scheinker disease, GSS); or complex syndromes of insomnia, hallucinations, motor abnormalities, and autonomic and endocrine disturbances

(fatal familial insomnia, FFI). Iatrogenic prion diseases can result from use of contaminated corneal or dura grafts, neurosurgical instruments, or cadaveric-derived pituitary hormones. Approximately 70 cases of an atypical form of CJD (new variant CJD) characterized by early age of onset and prominent initial neuropsychiatric and behavioral abnormalities followed by ataxia and progressive dementia have been reported, initially from England and France. It has been suggested, but not definitively established, that these cases may be the result of human exposure to food or other products derived from cattle infected with bovine spongiform encephalopathy ("mad cow disease"). CT and MRI are often normal but may show rapidly progressive atrophy or increased T2 signal in the basal ganglia (MRI). CSF cell counts and chemistries are normal. Both CSF and neuroimaging studies may help exclude other diagnoses. It has been reported that the presence in CSF of a specific protein (14-3-3) is suggestive but not diagnostic of CJD. EEG may show periodic sharp wave complexes in CJD, but these are absent or occur only rarely in GSS, FFI, and new variant CJD. Definitive diagnosis of sporadic forms of prion disease requires brain biopsy; findings include neuronal loss, astrogliosis, spongiform changes, absence of inflammatory response, and the presence, in GSS and new variant CJD, of typical plaques containing protease-resistant prion protein. The detection of protease-resistant prion proteins by immunoblotting or immunocytochemistry establishes the diagnosis. If the pt has a family history suggestive of inherited CJD, sequencing the prion protein gene may facilitate the diagnosis.(30)

Non-infectious meningitis causes include: Cancers, Systemic lupus erythematosus (lupus), Certain drugs, Head injury and Brain surgery (2)

History-Mechanism

Some suggest that Hippocrates may have realized the existence of meningitis (30) and it seems that meningism was known to pre-Renaissance physicians such as Avicenna (31)The description of tuberculous meningitis, then called "dropsy in the brain", is often attributed to Edinburgh physician Sir Robert Whytt in a posthumous report that appeared in 1768, although the link with tuberculosis and its pathogen was not made until the next century. (32)

It appears that epidemic meningitis is a relatively recent phenomenon (33) The first recorded major outbreak occurred in Geneva in 1805. (33) (34) Several other epidemics in Europe and the United States were described shortly afterward, and the first report of an epidemic in Africa appeared in 1840. African epidemics became much more common in the 20th century, starting with a major epidemic sweeping Nigeria and Ghana in 1905–1908. (33)

The first report of bacterial infection underlying meningitis was by the Austrian bacteriologist Anton Weichselbaum, who in 1887 described the meningococcus. (35)Mortality from meningitis was very high (over 90%) in early reports. In 1906, antiserum was produced in horses; this was developed further by the American scientist Simon Flexner and markedly decreased mortality from meningococcal disease. (36)(37)In 1944, penicillin was first reported to be effective in meningitis. (38) The introduction in the late 20th century of Haemophilus vaccines led to a marked fall in cases of meningitis associated with this pathogen, (39)and in 2002, evidence emerged that treatment with steroids could improve

the prognosis of bacterial meningitis.(40) (41) (30)World Meningitis Day is celebrated on the 24th of April each year.

Significance of Research

Bacterial meningitis requires bactericidal anti microbial agents that can cross the blood brain barrier in to the C S F. Most patients should be treated with intravenous anti biotics. Oral antibiotic should be used with caution because the dose and tissue levels tend to considerably lower than with parenteral agents. Antibiotic therapy should be initiated immediately after lumbar puncture. If imaging is performed before lumbar puncture, therapy should be initiated before the patient is sent for neuro imaging.

Most causes of viral meningitis are not preventable, although a good general precaution against viral meningitis is attention to handwashing since enteroviruses in particular usually enter the body via the hand to mouth route. Immunisation against mumps and measles (MMR) is offered to children at 12-13 months and 3 years of age as part of the routine childhood immunisation schedule. Immunisations are also available for some Flaviviruses such as tick-borne encephalitis and Japanese encephalitis, and are recommended for travellers to areas where the risk of these infections is high. Acyclovir can be used to treat HSV infection. However, there are no effective therapies for most viruses that cause meningitis (antibiotics are ineffective against viruses), so treatment is normally limited to easing the symptoms of the disease (for example painkillers for headache or anti-emetics to stop vomiting). Most people recover without any medical treatment within 5 days to a fortnight, but for some the recovery period is more prolonged.

The doctor may do a lumbar puncture. This is when a sample of cerebrospinal fluid (CSF) is taken from the spinal canal (the passageway through the back bones which contains the spinal cord). The sample of CSF will be examined and then sent for further laboratory testing. A lumbar puncture is important to confirm the diagnosis of meningitis, and to show which germ is causing the illness.

Where the Research Go Next

Tuberculous meningitis (TBM) presents a major health burden around the world, especially in individuals with concomitant HIV infection, in whom mortality is nearly 50%. Here, members of the TBM International Research Consortium summarize our current understanding of TBM pathogenesis, diagnosis and management, and discuss key avenues for future research.(41)

Bacteria have to overcome many obstacles to invade the meninges from the bloodstream. This Review considers how extracellular pathogens such as Neisseria meningitidis and Streptococcus pneumoniae bypass the blood-brain barriers, the understanding of which may lead to improved methods for delivering drugs into the brain.(42)

Community-acquired bacterial meningitis (inflammation of the meninges) is most commonly caused by Streptococcus pneumoniae or Neisseria meningitidis. Prevention (through vaccination) and early antibiotic treatment are essential to reduce morbidity and mortality of this medical emergency.(43) It has been proposed that viral meningitis might lead to inflammatory injury of the vertebral artery wall. (44)

The Meningitis Research Foundation is conducting a study to see if new genomic techniques can the speed, accuracy and

cost of diagnosing meningitis in children in the UK. The research team will develop a new method to be used for the diagnosis of meningitis, analysing the genetic material of microorganisms found in CSF (cerebrospinal fluid). The new method will first be developed using CSF samples where the microorganism is known, but then will be applied to CSF samples where the microorganism is unknown (estimated at around 40%) to try and identify a cause. (45)

It is a medical emergency. It requires immediate diagnosis and treatment. Untreated patients shows 100% mortality.

Symptoms include fever, neck stiffness, altered mental status. These symptoms develop over several hours to two days. G I T disturbances, the characteristic findings in bacterial meningitis Low glucose, High protein and WBC.

The patients may require C.T scan. Most patients should be treated with I.V Antibiotics.

Gram stain of organisms in the CSF should guide the selection of intravenous Antibiotics. Streptococcus pneumonia is the important cause of meningitis and pneumonia.

Most common cause of adult bacterial meningitis is Streptococcus pneumonia Neisseria meningitis cause purulent meningitis. It is the most common cause of meningitis between 2 to 18 years.

Haemophilus influenzae is the leading cause of meningitis especially in infants and young children. Streptococcus agalactiae causes meningitis in neonates Listeria monocytogenes is common in elderly, pregnant women.

Debate

Malaria and acute bacterial meningitis (ABM) are the leading infectious causes of febrile encephalopathy in malaria endemic settings. The clinical distinction of the two conditions is complicated by overlap in clinical features.(46)

823,348 people signed the petition to call on the government to act and vaccinate children under the age of 11 against this deadly strain of meningitis. Currently, the Meningitis B vaccine is available on the NHS for babies aged 2 months, followed by further doses at 4 months and a booster at 12 months. This is part of the childhood immunisation programme (since 1/9/2015). The new meningococcal B vaccine has been licensed in many jurisdictions in the past 2 years. Since 2014, national health authorities have implemented regionally focused campaigns to respond to either outbreaks of Men B invasive disease (e.g. In 2 American Universities) or durable high incidence of Men B disease in some countries (e.g. Quebec hyper-endemic regions). As of September 2015, more than 100,000 doses of the Men B vaccine have been administered - surveillance has confirmed the safety profile and vaccine acceptance in targeted populations has been high. The control of the outbreaks, with large reductions in the incidence of Men B disease, suggests the vaccine is effective against Men B.(47)

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